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ARNOLD & PORTER

Holly Logue Prutz
Holly_Prutz@aporter.com
202.942.5743
202.942.5999 Fax
555 Twelfth Street, NW
Washington, DC 20004-1206

1637

January 12, 2004

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Re: U.S. Patent Application No. 09/394,745
Filed: September 15, 1999
Title: **Nucleic Acid Molecules and Other Molecules Associated with Plants**
Applicants: Dane K. FISHER *et al.*
Atty. Docket No.: 16517.280/38-21(15454)B

Sir:

The following documents are forwarded herewith for appropriate action by the U.S. Patent and Trademark Office (USPTO):

1. Request for Reconsideration of Applicants' Petition under 37 C.F.R. § 1.181, with amended signature page, including Appendices A, B, and C; and

2. Return postcard.

Please stamp the postcard with the filing date of these documents and return it to our courier.

A prior identical copy of the attached Request for Reconsideration of Applicants' Petition under 37 C.F.R. § 1.181 was previously filed on January 12, 2004. The present copy is being filed with an amended signature page, but is otherwise identical to the previously-filed copy of the Request for Reconsideration having the same date.

Applicants do not believe any fees are due in conjunction with this filing. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned. However, if any fees are required in the present

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application, then the Commissioner is hereby authorized to charge such fees to Arnold & Porter Deposit Account No. 50-2387, referencing matter number 16517.280. A duplicate copy of this letter is enclosed.

Respectfully submitted,

David R. Marsh (Reg. No. 41,408)
Holly Logue Prutz (Reg. No. 47,755)

Attachments

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:			
Dane K. FISHER *et al.*		Art Unit:	1637
Appln. No.:	09/394,745	Examiner:	Young J. KIM
Filed:	September 15, 1999	Atty. Docket:	16517.280/38-21(15454)B
Title:	**Nucleic Acid Molecules and Other Molecules Associated with Plants**		

Request for Reconsideration of Applicants' Petition under 37 C.F.R. § 1.181

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Responsive to the Decision on Petition under 37 C.F.R. § 1.181(a)(3) mailed November 12, 2003 ("Petition Decision"), Applicants hereby request reconsideration of the Petition Decision and request the Commissioner to invoke his supervisory authority and require the Examiner to reopen prosecution and examine the invention claimed by Applicants. It is not believed that any fees are required in conjunction with this Request, however, should any fees be deemed necessary, permission to charge such fees is given in the accompanying transmittal letter. This Request is timely filed within two months of the mailing date of the Decision.

The facts of the present application and the previously-filed petitions are established in the record and need not be repeated in their entirety herein. However, for convenience, a brief overview of the facts pertinent to the present Request is attached hereto as Appendix A. A copy of the currently pending claims, as presently pending in the application, is attached hereto as Appendix B. The complete text of claims 8-10, as originally filed in the Preliminary Amendment are also attached hereto as Appendix C.

A. Summary of Arguments

On November 12, 2003, the Office issued the Petition Decision that is the subject of the present Request. In that Petition Decision, the Office dismissed Applicants' Petition Under 37 C.F.R. § 1.181 filed July 9, 2003, as premature.[1] The crux of the Office's position is the contention that "[s]ince no claim has been withdrawn from consideration. . . as a result of the restriction requirement that is the subject of the present petition, the examiner is not refusing to examine any claim in the above-identified application as a result of the restriction requirement. . ." Petition Decision at page 2. In that regard, the Office further contends that "an affirmance of the rejection of claims 8 through 11 under 35 U.S.C. § 101 or under 35 U.S.C. § 112, ¶ 1, would moot any complaint concerning how these claims have been treated relative to the prior art."[2] *Id.* In short, the Office asserts that because claims 8-11 are still pending in the present application, and because claims 8-11 have been rejected under 35 U.S.C. §§ 101 and 112, first paragraph, it is not necessary to examine all of the nucleic acid molecules included in Applicants' claimed microarray until these rejections have been overcome.

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[1] In the petition under 37 C.F.R. § 1.181, Applicants petition the Commissioner to invoke his supervisory authority and require the Examiner to reopen prosecution of the present application to examine the full scope of invention claimed by Applicants. The Office has twice issued decisions prior to the petition under 37 C.F.R. § 1.181, denying Applicants' requests to withdraw the restriction requirement applied to claim 8 and its dependents "to select one combination [of nucleic acid molecules] for examination", and to restrict examination of the claimed invention "to only the elected combination." Office Action mailed December 19, 2000 ("Restriction Requirement"), at pages 2-3.

[2] On March 13, 2003, Applicants filed an Appellant's Brief addressing the outstanding rejections under 35 U.S.C. §§ 101 and 112. Applicants' filed a second Appellant's Brief on June 30, 2003, addressing the separate rejection of claims 8-11 for refusal to examine the claimed invention.

This position cannot be sustained. It completely ignores that the §§ 101 and 112 rejection is based on the examination of a ***single sequence*** within the claimed microarray. Although the Office professes to have examined and rejected ***an*** invention, the Office has ***not*** examined ***Applicants' claimed invention***. Rather, the Office has embarked on a piecemeal examination which perverts the examination process by failing to take into account ***Applicants' claimed invention*** and instead treating a ***different*** (single sequence based) invention arbitrarily imposed upon Applicants through the Office's improper restriction policy. While that indeed produced a rejection under §§ 101 and 112, the rejection fails to account for the invention ***as a whole.*** As explained more fully below, when ***Applicants' claimed invention as a whole*** (rather than the single sequence based invention arbitrarily imposed upon Applicants) is examined, the §§ 101 and 112 analysis and inquiries, as well as their proper resolution, all change. Presently, the §§ 101 and 112 rejections have in reality been issued against a piece of a single claim – a claim that the Office has arbitrarily required to be divided up and treated in fragments. But the "totality of the resulting fragmentary claims would not necessarily be the equivalent of the original claim" and thus, the rejections issued against the fragmentary claim will not reflect an examination of the originally claimed invention. *Appln. of Weber*, 580 F.2d 455, 458-459, 198 U.S.P.Q. 328, 332 (C.C.P.A. 1978). As such, the Petition Decision's contention that there has been no refusal to examine Applicants' invention is plainly wrong.

For that reason, the Petition Decision is also way off base in its inappropriate reliance on a very broad and general truism that the Office may issue rejections in any order that it sees fit and Applicants do not have "the right to have their applications examined in any particular manner." Petition Decision at page 2. This assertion ignores the fact that Applicants have not had ***their*** invention examined ***at all***. In addition, it wrongly seeks to convert that truism into a right of the Office to arbitrarily establish a gauntlet of piecemeal examination which prevents Applicants from challenging the Office's restriction policies in an appropriate forum. The cases relied upon in the

Petition Decision simply do not support any such right and are wholly inapplicable to the facts of the present case. It is pure sophistry to rely on those cases as a pretense for turning a blind eye to the plain fact that ***Applicants' claimed invention*** has not been examined and for disregarding well-established law that restriction requirement ***within*** a single claim is improper.[3] Applicants have set forth what they regard as their invention, and the Office has simply refused to examine ***that*** invention.

B. Detailed Arguments

(1) Examination of the Claimed Invention Results in a Different Analysis and Resolution Under 35 U.S.C. §§ 101 and 112

The Petition Decision baldly asserts that "[s]ince no claim has been withdrawn from consideration in the above-identified application as a result of the restriction requirement . . . the examiner is not refusing to examine any claim in the above-identified application as a result of the restriction requirement". Petition Decision at page 2. This statement misses the point – Applicants herein are not contesting a restriction ***between*** inventions embodied in ***separate*** claims, but rather Applicants assert that the Office has improperly imposed a restriction requirement ***within*** a claim directed to a ***single*** invention.[4] Furthermore, because the restriction requirement fragmented the invention embodied in this single claim, ***Applicants' invention*** was never examined under 35 U.S.C. §§ 101 and 112, first paragraph.

Therefore, because the invention claimed has never been examined by the Office, it is likewise inconceivable that "an affirmance of the rejection of claims 8 through 11 under 35 U.S.C. § 101 or under 35 U.S.C. § 112, ¶ 1, would moot any complaint concerning how these

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[3] *Appln. of Weber*, 580 F.2d 455, 458-459, 198 U.S.P.Q. 328, 332 (C.C.P.A. 1978); *Appln. of Haas*, 580 F.2d 461, 464, 198 U.S.P.Q. 334, 336-337 (C.C.P.A. 1978); *Appln. of Haas*, 486 F.2d 1053, 1056, 179 U.S.P.Q. 623, 625 (C.C.P.A. 1973).

[4] The Office has ***admitted*** as much:

> First Applicants argue that the examiner, by forcing applicants to elect a single combination of sequences for examination, has narrowed the scope of the claims. ***This is correct, and that was the purpose of the restriction requirement.***

Petition Decision mailed May 12, 2003, at page 2 (emphasis added).

claims have been treated relative to the prior art." Petition Decision at page 2. It is not simply the treatment of the claims relative to the prior art that is at issue in this application. Rather, the issue that is ignored by the Petition Decision is that examination of the invention ***claimed by Applicants*** changes the analysis and inquiry under 35 U.S.C. §§ 101 and 112, first paragraph, and their proper resolution.

The Office admits that it agreed to examine, and in fact ***only*** examined SEQ ID NO: 5893 for novelty.[5] However, the outstanding rejections under 35 U.S.C. §§ 101 and 112, first paragraph, despite being broadly asserted as directed to "the claimed combination of nucleic acids", and to "microarrays in general",[6] in reality only consider the invention in the context of one which always includes SEQ IN NO: 5893, as is evidenced in the Petition Decision mailed February 14, 2003, at page 2.[7] Thus, despite attempts by the Office to phrase the outstanding rejections as though they apply to "the claimed combination of nucleic acids", the Office has effectually examined the invention as if it were directed to a single SEQ ID NO. And, as such, that Office has arbitrarily imposed ***this*** invention on Applicants through its improper restriction practice. Moreover, even if the outstanding rejections were directed to the single combination of SEQ ID NOs, which always must include SEQ ID NO: 5893, this would still not result in an analysis of the invention ***claimed by Applicants*** under 35 U.S.C. §§ 101 and 112. Rather, it amounts to piecemeal examination of the whole invention and an examination of fragmentary claims:

> [i]f an applicant submits a number of claims, it may well be that pursuant to a proper restriction requirement, those claims will be dispersed to a number of applications. . . If, however, a single claim is required to be divided up and presented in several applications, that claim would never be considered on its

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[5] *See, e.g.,* Office Action mailed March 18, 2002, at page 10.

[6] *See, e.g.,* Office Action mailed March 18, 2002; and Examiner's Answer mailed May 23, 2003.

[7] This petition decision declares "Applicants may claim as many combinations as they wish. So long as the claimed combinations include SEQ ID NO: 5893, they are free of the prior art and no further search would be required to examine such claims."

> merits. The totality of the resulting fragmentary claims would not necessarily be the equivalent of the original claim.

Appln. of Weber, 580 F.2d 455, 458.

The microarray claimed by Applicants, which contemplates the ability to include or exclude any nucleic acid molecule comprising any one or more of the nucleic acid sequences that is a member of the group of nucleotide sequences set forth in claim 8, is much like a piano containing 88 different keys. Although each of the keys may appear similar, it is the combination of all 88 keys, and the ability of the player of the piano to select which key or keys to play at a given moment, that lends itself to the creation of music. While one key may be sufficient to play a single note, it is the combination of seven notes, flat and sharp tones for each note, and a range of eight octaves that creates the ability of one to play a concerto by Mozart or a sonata by Beethoven.

The Office's improper restriction policy has divided that piano into a piano containing a single key, and the usefulness of a piano with only one key is distinguishable from that of a piano having all 88 keys. There would be no ability for the piano player to select another key or combination of keys to play which did not include that single key. Such a restriction on the player's ability would not lend itself to the creation of music. Rather, it is the ability of the player of the piano to select which keys to include or exclude at specific points during a performance that lends itself to the full advantages of the piano, not simply the inclusion of a single key. While a piano with only one key may be useful as a mere tuning instrument, it would not offer the same advantage that a piano with all 88 keys would.

In much the same way, Applicants' invention contemplates the ability of the user of the claimed microarray to select from among thousands of collections and combinations of nucleic acid molecules when determining how best to screen a sample for the detection of a desired nucleic acid molecule or molecules. Piecemeal examination disregards this selectivity by the user, which is embodied in Applicants' invention. Examination of a single nucleic acid sequence, or a single combination of nucleic acid sequences, or even examination of various

combinations of nucleic acid sequences which always ***must*** include a ***single*** nucleic acid sequence, as selected by the Office and ***not*** the user of the claimed invention, nullifies the advantages of the claimed invention. Rather than allowing the player of the piano to select which key or keys to play at a given point during a performance, the Office would restrict the player to a single key. As such, examination of the invention ***examined by the Office*** results in a radically different analysis than examination of the ***invention claimed by Applicants***. The Office saw fit to examine a single key of the piano whereas Applicants have repeatedly stated that this single key is ***not*** the invention claimed.

It is not surprising that the analysis, inquiry, and resolution of the current rejections under 35 U.S.C. §§ 101 and 112 changes dramatically when the invention ***claimed by Applicants***, rather than one arbitrarily imposed by the Office, is examined. In much the same way as a single key on a piano cannot account for the advantages that instrument has to offer, a single nucleic acid sequence or single combination of nucleic acid sequences which always must include a single nucleic acid sequence as selected by the Office, cannot offer the same uses considered in the entirety of the claimed microarray.

One skilled in the art can use the claimed microarray to monitor changes in expression of a gene that encompasses a single nucleic acid sequence in combination with other selected sequences. Each nucleic acid molecule on Applicants' claimed microarray contributes to the ability of the scientist using the claimed microarray to examine any one of the claimed nucleic acid sequences in conjunction with other nucleic acid sequences. The combination of which nucleic acid molecules to include or exclude on the microarray is within the ability of the user of Applicants' claimed microarray. It is not up to the Office to contemplate what the scientist may find useful in his studies, any more than it is within the ability for a piano designer to design a piano with one key and determine that this should be sufficient for a performance by even the most skilled pianist.

Thus, much as a piano with a single key does not represent the same utility as a piano with 88 keys, examination of a single nucleic acid sequence or even a single combination of nucleic acid sequences which always must comprise a single nucleic acid sequence, does not amount to examination of the ***whole invention*** claimed by applicants. To suggest, as the Office does, that Applicants' invention has been examined or that an affirmance of the rejections under 35 U.S.C. §§ 101 and 112, first paragraph, would moot any complaint concerning examination of the invention claimed by Applicants is manifestly wrong.

In addition to resulting in an incorrect analysis of the invention, the improper restriction requirement precludes Applicants from presenting their integrated invention in another application. *Cf. Appln. of Hengehold,* n.11, 440 F.2d 1395, 1404, 169 U.S.P.Q. 473, 480, 58 C.C.P.A. 1099, 1110 (C.C.P.A. 1971) (where a restriction requirement was issued between claims directed to separate inventions, the applicant was not prevented from presenting claims directed to a separate invention in a subsequent application). The improper restriction requirement did more than just divide Applicants' invention, it destroyed the invention as a whole.

In the present application, the Office has examined a single key, not the entire piano, out of context of the entire invention claimed. Examination of a single nucleic acid molecule, or even a combination of nucleic acid molecules that always must include a single nucleic acid molecule, cannot amount to an examination of the claimed invention. Applicants' invention has been divided up into fragments and subject to piecemeal examination such that the claimed invention has never and will never be examined on its merits under the Office's incorrectly applied restriction polices. To claim, as the Office attempts to do, that such an examination amounts to examination of the claimed invention is ludicrous.

(2) It is an Abuse of Discretion for the Office to Establish a Policy Aimed at Creating a Gauntlet of Piecemeal Examination

The Office attempts to support its position that Applicants' Petition under 37 C.F.R. § 1.181 contesting the restriction requirement is "premature" by relying on the assertion that

> [w]hile Office personnel are to state all non-cumulative reasons and bases for rejecting claims in the first Office action under the Office's 'compact prosecution' policy, this policy is a matter of internal Office management and does not vest applicants with the right to have their applications examined in any particular manner. The Office's reviewing court has indicated that it is permissible and even appropriate to defer imposition of any applicable art based rejection until the non-prior art based rejections have been resolved.

Petition Decision at page 2, *citing In re Steele*, 305 F.2d 859, 134 U.S.P.Q. 292 (C.C.P.A. 1962). While ignoring the fact that Applicants' invention has not been examined ***at all*** as a result of the improper restriction requirement, the Office seeks to convert this truism into a right of the Office to arbitrarily establish a policy of piecemeal examination that does not amount to an examination of the claimed invention. Such a policy by the Office is a clear abuse of discretion and establishes a war of attrition on applicants who seek to challenge the Office's restriction policies and politics, and creates a barrier to fair judicial review by imposing costs and delays that many applicants cannot bear. If this truism were to be facially accepted, as the Office would like it to be, the Office could contend that it has a right to reject Applicants' invention under 35 U.S.C. §§ 101 and 112, first paragraph, force Applicants to go through a lengthy appeal process, then, if Applicants are able to prevail on these rejections, the Office ***may still*** continue to prevent a court from reviewing the rejection for refusal to examine the ***invention claimed*** by imposing additional rejections as it sees fit.

That the Petition Decision purports to find support for its position in *In re Steele* is wholly unconvincing in light of the specific facts of that case. A careful reading of *Steele* does ***not*** support any broad contention that it is "permissible and even appropriate to defer imposition of any applicable art based rejection until the non-prior art based rejections have been resolved." Petition Decision at page 2. Rather, in *Steele*, the Court merely overturned the Board's

affirmance of the examiner's rejection of the claims of a patent application under 35 U.S.C. § 103, for reasons that are not present in this case. The *Steele* Court determined that the "analysis of the claims indicat[ed] that considerable speculation as to meaning of the terms employed and assumptions as to the scope of such claims were made by the examiner and the board." *In re Steele*, 305 F.2d 859, 862. More particularly, the Court found that a rejection over the prior art should not be based on "speculations and assumptions" as to the proper interpretation of the claims, and held that the claims should be examined for compliance with 35 U.S.C. § 112, second paragraph, before determining whether or not a rejection over the prior art could be rendered based on guesswork. *Id.*

These circumstances are not present in this case, nor does the outcome have any application to the situation created by the Office's improper restriction policies. Applicants' claims have not been rejected over the prior art, nor has it been asserted by the Office that Applicants' claims would lack clarity as to the scope of the claimed invention in light of the disclosure of the specification. More importantly, however, Applicants are not, as has been asserted in the Petition Decision, requesting that the Office consider additional art-based rejections in the present application; rather, Applicants are requesting their right to examination of the ***invention claimed***. As stated above, the current rejections under 35 U.S.C. §§ 101 and 112, first paragraph, do not take into account Applicants' claimed invention but rather an analysis of a ***different*** invention arbitrarily defined by the Office. The Office may ***not*** rely on the holding in *Steele* to support a position that it may issue rejections as it sees fit when those rejections do not take into account the ***claimed invention***.

Nor did *Steele* establish a policy that allows the Office to arbitrarily issue rejections in an order most beneficial to its current policies. There is simply ***no*** support for the broad proposition that "it is permissible and even appropriate to defer imposition of any applicable art based rejection until the non-prior art based rejections have been resolved." Rather, the Court has

stated that "a careful statement of the precise statutory grounds of rejection is essential in all cases. . ." *In re Sinex,* 309 F.2d 488, 492, 135 U.S.P.Q. 302, 305 (C.C.P.A. 1962). It is not permissible for the Office to pervert the examination process by intentionally ignoring the rejection of Applicants' invention by refusal of the Office to examine ***that*** invention and by burying the issue within other rejections. The Office has no right to arbitrarily establish a gauntlet of piecemeal examination which prevents Applicants from challenging the Office's restriction practice in an appropriate forum.

It is also absurd to state, as the Petition Decision does, that Applicants have not been " 'adversely affected or aggrieved by agency action' by the Office's failure to enter a prior art rejection." Petition Decision at page 2, *quoting Animal Legal Defense Fund v Quigg,* 932 F.2d 920, 930, 18 U.S.P.Q.2d 1677, 1686 (Fed. Cir. 1986). As with *Steele*, the reliance upon this case by the Office in support of such a statement is conspicuously out of place with the facts of the present case. In *Quigg,* the plaintiffs-appellants were various organizations who collectively challenged a notice issued by the Office falling within the interpretative exception under 5 U.S.C. § 553 to the public notice and comment procedures. That notice considered "non-naturally occurring, non-human multicellular organisms, including animals, to be patentable subject matter within the scope of 35 U.S.C. § 101. . ." *Quigg,* 932 F.2d 920, 922. The appellants did not assert any "adverse effect on any individual's rights to benefits under the patent statute," rather, they "assert[ed] a right, as members of the public particularly interested in animals, to sue for what they perceive to be an unwarranted interference with the discretionary judgment of an examiner." *Id.* at 929.

Unquestionably, this is not the case in the present application. Here, the treatment of the present application by the Office has a direct impact on the rights of Applicants. *Cf. Quigg,* 932 F.2d 920, 930 ("we find nothing in the law which gives rise to a right in ***nonapplicants*** to object to the way in which patent applications of others are prosecuted.") (Emphasis added.) It is

inconceivable to suggest, as the Office attempts to do, that Applicants would have no standing to challenge the actions of the Office in a situation where the Office has refused to examine ***their invention***.

Thus, while it may be generally correct that examination policy in the Office "is a matter of internal Office management and does not vest applicants with the right to have their applications examined in any particular manner", this general truism cannot be seized upon and converted by the Office to create an arbitrary policy that establishes a barrier for Applicants to challenge the refusal by the Office to examine the ***claimed invention***. The Office may not hide the fact that the restriction requirement within the claimed invention amounts to an improper rejection by relying on a doctrine that prevents any challenge of the Office's current restriction practice as arbitrarily and overzealously applied to biotechnology inventions. Because restriction practice is a petitionable matter, no recourse may be left for Applicants to immediately appeal the *de facto* rejection of the claimed invention. The Office is thus able to continue, unfettered, a policy of rejecting Applicants' invention through restriction practice, in clear contradiction to precedential holdings, while usurping the jurisdiction of the Board of Patent Appeals and Interferences and the Federal Circuit to review the policy articulated in M.P.E.P. § 803.04 and the Office's application thereof.

It is a fallacy to rely on the cases cited in the Petition Decision to disregard Applicants' repeated position that the ***claimed invention*** has not been examined and the improper restriction requirement ignores well-established law. Applicants have set forth what they regard as their invention and the Office has simply refused to examine ***that*** invention. As such, the ***only*** rejection by the Office of Applicants' claimed invention is the improper refusal to examine that invention.

C. Conclusion

In view of the arguments above, Applicants specifically petition the Commissioner to review and require withdrawal of the restriction requirement and return this application to the Examiner with instructions to re-open prosecution and examine the full scope of the claimed invention.

Respectfully submitted,

Thomas E. Kelley

Thomas E. Kelley (Reg. No. 29, 938)
by David R. Marsh (Reg. No. 41,408)
by Holly Logue Prutz (Reg. No. 47,755)
by Holly Logue Prutz

Date: January 12, 2004

MONSANTO COMPANY
62 Maritime Drive
Mystic, CT 06355
860-572-5274 telephone
860-572-5280 facsimile

ARNOLD & PORTER
The Thurman Arnold Building
555 Twelfth Street, N.W.
Washington, DC 20004-1206
202.942.5000 telephone
202.942.5999 facsimile

Appendix A: Summary of Facts

1. Application Serial No. 09/394,745, filed September 15, 1999 ("Application"), discloses 57,264 nucleic acid sequences for expressed sequence tags (ESTs,) *i.e.*, short sequences of genes of the plant *Zea mays* (corn) obtained by sequencing from the 5' end of cDNA clones. The sequence listing discloses SEQ ID NOs: 1 – 57264. Application at page 9, lines 24 through 26 and page 91, line 5 through page 99, line 26 (Examples 1-2).

2. The Application was originally filed with 7 claims directed to nucleic acid molecules and transformed plants. In a preliminary amendment filed on October 10, 2000 ("Preliminary Amendment"), Applicants canceled all of the original claims and added new claims 8-11. Claim 8 and its dependents were directed, in general, to "a microarray having a substrate with a surface comprising 10^3 nucleic acid molecules or more where at least 10% of the nucleic acid molecules are different and at least about 250 nucleotide residues and complementary to a nucleic acid molecule having a sequence selected from a Markush group consisting of [497 nucleotide sequences]".[8]

3. The Remarks section of the Preliminary Amendment explains that Applicants' representative, Linda T. Parker, carried out a computer search on November 3, 1999, of the nonredundant nucleotide database posted by the National Center for Biotechnology Information (NCBI) (ftp://ftp.ncbi.nlm.nih.gov/blast/db/ntz). Preliminary Amendment at page 14. The computer search involved a BLASTN query using the default parameters and SEQ ID NO: 5746 through SEQ ID NO: 8666 as the query sequences. A copy of the BLASTN output was submitted on CD-ROM with the Preliminary Amendment. *Id.* at 15. Based on the output of the BLASTN analysis, the original set of 2961 sequences was reduced to the 497 nucleotide sequences listed in the claims.[9]

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[8] The complete text of claims 8-11, as presently pending in the application, are attached hereto as Appendix B. The complete text of claims 8-11, as originally filed in the Preliminary Amendment, are attached hereto as Appendix C.

[9] The selection of the 497 nucleotide sequences included in claims 8-11 was based on identifying, from the original set of 2921 sequences, only those sequences that were greater than 400 nucleotides in length and either had no matches to any public sequence in the queried database or matched for the top hit (best E value; definition available at http://www.ncbi.nlm.nih.gov/Education/BLASTinfo/glossary2.html) to a public sequence in the queried database in only a single high scoring pair of less than 100 nucleotides where the match had an expectation (E value) greater than 1E-3.

4. In the Office Action mailed December 19, 2000 ("Restriction Requirement"), the Examiner restricted the application to one of two groups, with Group I consisting of claims 8-10, drawn to a microarray containing a set of nucleic acid molecules that were not fully characterized, and Group II consisting of claim 11, drawn to a microarray containing a defined set of nucleic acid molecules. Restriction Requirement at page 2. The Examiner also recognized that the "different inventions contain different and distinct sets of nucleic acid molecules and therefore have different structures and functions." *Id.*

5. The Restriction Requirement further stated that in claims 8-10 the subset of nucleic acid sequences "are not clearly defined because the subset is recited as containing 1000 nucleic acid molecules, only 100 of them being unique, selected from a group of approximately 400 nucleic acid molecules. It would be an undue search burden to perform a search on every combination of 100 nucleic acid molecules selected from a set of 400 molecules." Restriction Requirement at page 2. The Restriction Requirement went on to state "[i]t is noted that if applicants claim a combination of nucleotide sequences, the presence of one novel and nonobvious sequence within the combination will render the entire combination allowable." *Id.* The Restriction Requirement further states "a combination of nucleotide molecules comprising a defined group of nucleotide molecules is required." *Id.* at pages 2-3. Thus, the Examiner required that should Applicants select Group I (claims 8-10) for examination, then "Applicants are required to select one combination for examination" and examination "will be restricted to only the elected combination."[10] *Id.* at page 3.

6. In a Response to Restriction Requirement dated April 17, 2001 ("Response to Restriction Requirement"), Applicants provisionally elected, with traverse, the subject matter of Group I, *i.e.*, claims 8-10. Response to Restriction Requirement at page 1. In addition, Applicants provisionally elected, with traverse, the first 100 sequences in the Markush group in response to the additional restriction requirement, or election of species, imposed by the Examiner. *Id.* at pages 2-3. Applicants also expressed their belief that it would not pose an undue burden on the

[10] Applicants assert that this reading of claim 8 and its dependents is improper. The Examiner's requirement that Applicants elect a single combination for examination reflects an improper understanding of the invention disclosed in claim 8.

Patent Office to examine all of the sequences listed in the claims and, reiterating remarks in the Preliminary Amendment, pointed out that

> It took applicants' representative less than 10 minutes to set up the BLASTN search. After the BLASTN search was completed, Applicants' representative spent approximately 2 hours examining and parsing the BLASTN output with the purpose of selecting those sequences which either had no matches to any sequence in the queried database or which fulfilled other criteria. In this case, the Examiner is being asked to examine only 498 [sic – 497] sequences, rather than approximately 3000. ... To further avoid any undue search burden the PTO is encouraged to refer to the preliminary amendment of October 10, 2000 in which applicant [sic] submitted a copy of the BLASTIN output on CD-ROM.

Id. at page 2.

7. In the Office Action mailed May 21, 2001 ("First Office Action"), the Examiner alleged that Applicants' response to the restriction requirement was not fully responsive because although "it appears that Applicants have elected a specific combination of nucleic acids, it is not definite what the elected SEQ ID Numbers are." First Office Action at page 2. The Examiner also required Applicants to "specifically recite, on the record, all one hundred SEQ ID numbers that are elected." *Id.*

8. Applicants filed a Reply to Detailed Action on July 3, 2001 ("Reply"), traversing the Patent Office position that the Response to the restriction requirement was not fully responsive. Reply at page 1. It was also reiterated that Applicants had elected with traverse Group I, claims 8-10, "each of which is characterized by the same Markush group of 498 [sic – 497] nucleotide sequences," and that in response to the further restriction requirement, or the election of species as the case may be, Applicants had elected the "first 100 sequences in the Markush group." *Id.* at pages 1-2. To facilitate prosecution, Applicants explicitly recited the 100 sequences from the Markush group selected as the species for examination. *Id.* at pages 2-3.

9. In a second Office Action mailed March 18, 2002 ("Second Office Action"), the Examiner, upon further consideration, withdrew the restriction requirement between Groups I and II and allowed all of the pending claims to be examined together. Second Office Action at page 2. However, in addressing Applicants' repeated objections to the restriction requirement for electing a combination, and Applicants' argument that they had performed a search via BLASTIN for 2921 sequences in a reasonable time frame, the Examiner responded "this

argument is not found persuasive because the PTO does not conduct sequence searches in like manner. For each claimed SEQ ID Number, the Office must perform a sequence search, for each SEQ ID Number, on a commercial database (which includes multiple databases), PTO in-house database, and the issued-patent database," and thus there would be an enormous search burden. *Id.* The Examiner further stated that "the examination of SEQ ID Numbers will not go beyond the 100 SEQ ID Numbers." *Id.* (emphasis added). The Second Office Action also recited rejections of the claims under 35 U.S.C. §§ 101 and 112, first paragraph.

10. In an Amendment and Response dated June 18, 2002 ("Amendment"), Applicants amended all of the pending claims to reflect the 100 elected sequences and to correct typographical errors. Amendment at pages 1-3. Applicants further maintained their traversal with respect to the requirement for electing a combination and the restriction requirement limiting the examination to 100 SEQ ID Numbers. *Id.* at page 4. Applicants also pointed out that "[a]rrays of nucleic acid sequence[s] are commonly employed where a single array on a solid support contains thousands of separated nucleic acid sequences. To require an applicant to file hundreds of applications to cover a single product would serve only to effectively deprive applicant of patent rights on his invention." *Id.* Applicants also argued against the outstanding rejections of the claims under Sections 101 and 112.

11. In a final Office Action mailed on September 11, 2002 ("Final Office Action"), the Examiner maintained the rejections of the claims under Sections 101 and 112. The Examiner acknowledged Applicants' traversal "with regard to the restriction of the claims into a specific combination of 100 SEQ ID Numbers". Final Office Action at page 2. The Examiner further stated that

> Applicants are advised that the actual combination of 'one hundred' SEQ ID Numbers was selected by Applicants, and was not required by the Examiner. Applicants were requested to elect a single combination of nucleic acids to which Applicants have elected the 'first one hundred' SEQ ID Numbers as the elected combination. In other words, Applicants could have elected all of the recited SEQ ID Numbers as the combination to be examined. However, it was Applicants who have decided to elect the first 100 SEQ ID Numbers as the elected combination.

Id. The Examiner also acknowledged that

> It appears Applicants are traversing the restriction requirement wherein Applicants were required to elect a single combination. If Applicants are traversing that such requirement should not have been made, Applicants are referred to MPEP 803.04, example C, wherein it explicitly states that such combination claims would be subject to restriction requirement wherein Applicants will be required to 'select one combination for examination'. However, if Applicants are traversing at [sic] the fact that only 100 SEQ ID Numbers were examined as the elected combination, Applicants are advised that it was Applicants who have decided to elect the first 'one hundred SEQ ID Numbers' as the combination to be examined.

Final Office Action at page 2.

12. On January 10, 2003, Applicants filed a Petition under 37 C.F.R. § 1.144 ("First Petition"), arguing that the restriction requirement was contrary to law because it denied Applicants their statutory right to examination of what they regard as their invention. Applicants pointed out that the restriction requirement and the application of the policy set forth in M.P.E.P. §803.04 divided the claimed invention and redefined it into a different invention. First Petition at pages 9-14.

13. Applicants' First Petition was denied in a Petition Decision mailed February 14, 2003 ("First Decision"). This First Decision stated that "the examiner has not rewritten anything." First Decision at page 2. However, the First Decision contradictorily stated that

> Applicants may claim as many combinations as they wish. So long as the claimed combinations include SEQ ID NO: 5893, they are free of the prior art and no further search would be required to examine such claims.

Id.

14. On March 13, 2003, Applicants filed an Appellant's Brief ("First Appeal Brief"), addressing the outstanding rejection of claims 8-11 under 35 U.S.C. § 101 and § 112, first paragraph. The First Appeal Brief did not address the rejection of claims 8-10 by virtue of the Office's refusal to examine the claimed invention.

15. On April 14, 2003, Applicants filed a Request for Reconsideration of Applicants' Petition under 37 C.F.R. § 1.144 ("First Request"), which addressed the points presented in the First Decision. The First Request reiterated the fact that "the restriction to a single grouping of nucleic acid molecules redefines the claimed invention and effectively denies Applicants' statutory right to examination of what they regard as their invention." First Request at page 6.

16. The Office issued a second Petition Decision on May 12, 2003 ("Second Decision"), again denying Applicants' request to remove the restriction requirement and examine the full scope of the claimed invention. In particular, the Second Decision acknowledges that the invention examined by the Office was not the same invention claimed by Applicants:

> First, applicants argue that the examiner, by forcing applicants to elect a single combination of sequences for examination, has narrowed the scope of the claims. This is correct, and that was the purpose of the restriction requirement.

Second Decision at page 2. As such, the Office confirmed that the invention claimed by Applicants was never examined, and was refused examination.

17. An Examiner's Answer was mailed on May 23, 2003, addressing the arguments presented by Applicants in the First Appeal Brief. The restriction requirement was not addressed in this paper.

18. By virtue of the Second Decision, Applicants' claims 8-10 had now been twice rejected by the Office's refusal to examine the claimed invention. *See* 37 C.F.R. § 1.191(a). In response, Applicants appealed the rejection of these claims by filing a second Notice of Appeal and second Appellant's Brief ("Second Appeal Brief") on June 30, 2003. The Second Appeal Brief specifically addressed the rejection of claims 8-10 by virtue of the Office's refusal to examine the claimed invention, and argued that the restriction requirement was inappropriately applied within a single claim, not within separate claims directed to different inventions.

19. Upon submitting their Second Appeal Brief, Applicants were invited to submit another petition directly to Stephen Kunin, Deputy Commissioner for Patent Examination Policy. Accepting this invitation, on July 9, 2003, Applicants submitted a Petition under 37 C.F.R. § 1.181 ("Second Petition") again addressing the inappropriate restriction requirement within a single claim and the Office's refusal to examine the claimed invention.

20. The Office denied Applicants' Second Petition in a Decision on Petition Under 37 C.F.R. § 1.181(a)(3) mailed November 12, 2003 ("Petition Decision"). This Petition Decision prompted the present Request and the issues raised by this Petition Decision are the subjects of the present Request.

Appendix B: Pending Claims

8. A microarray comprising a substrate with a surface comprising 10^3 nucleic acid molecules or more where at least 10% of the nucleic acid molecules are comprised of different sequences and at least about 250 nucleotide residues and complementary to a molecule comprising a sequence selected from the group consisting of SEQ ID NO: 5776, SEQ ID NO: 5781, SEQ ID NO: 5782, SEQ ID NO: 5783, SEQ ID NO: 5785, SEQ ID NO: 5787, SEQ ID NO: 5800, SEQ ID NO: 5804, SEQ ID NO: 5815, SEQ ID NO: 5818, SEQ ID NO: 5821, SEQ ID NO: 5823, SEQ ID NO: 5828, SEQ ID NO: 5830, SEQ ID NO: 5832, SEQ ID NO: 5836, SEQ ID NO: 5838, SEQ ID NO: 5840, SEQ ID NO: 5845, SEQ ID NO: 5849, SEQ ID NO: 5850, SEQ ID NO: 5851, SEQ ID NO: 5856, SEQ ID NO: 5859, SEQ ID NO: 5863, SEQ ID NO: 5868, SEQ ID NO: 5871, SEQ ID NO: 5874, SEQ ID NO: 5875, SEQ ID NO: 5877, SEQ ID NO: 5893, SEQ ID NO: 5896, SEQ ID NO: 5901, SEQ ID NO: 5908, SEQ ID NO: 5909, SEQ ID NO: 5920, SEQ ID NO: 5922, SEQ ID NO: 5926, SEQ ID NO: 5928, SEQ ID NO: 5929, SEQ ID NO: 5931, SEQ ID NO: 5936, SEQ ID NO: 5937, SEQ ID NO: 5939, SEQ ID NO: 5941, SEQ ID NO: 5944, SEQ ID NO: 5945, SEQ ID NO: 5950, SEQ ID NO: 5955, SEQ ID NO: 5960, SEQ ID NO: 5961, SEQ ID NO: 5963, SEQ ID NO: 5964, SEQ ID NO: 5968, SEQ ID NO: 5973, SEQ ID NO: 5974, SEQ ID NO: 5991, SEQ ID NO: 5994, SEQ ID NO: 5999, SEQ ID NO: 6000, SEQ ID NO: 6001, SEQ ID NO: 6005, SEQ ID NO: 6006, SEQ ID NO: 6007, SEQ ID NO: 6011, SEQ ID NO: 6017, SEQ ID NO: 6018, SEQ ID NO: 6022, SEQ ID NO: 6023, SEQ ID NO: 6026, SEQ ID NO: 6030, SEQ ID NO: 6033, SEQ ID NO: 6042, SEQ ID NO: 6046, SEQ ID NO: 6059, SEQ ID NO: 6063, SEQ ID NO: 6065, SEQ ID NO: 6066, SEQ ID NO: 6089, SEQ ID NO: 6091, SEQ ID NO: 6098, SEQ ID NO: 6106, SEQ ID NO: 6107, SEQ ID NO: 6110, SEQ ID NO: 6117, SEQ ID NO: 6121, SEQ ID NO: 6124, SEQ ID NO: 6131, SEQ ID NO: 6137, SEQ ID NO: 6141, SEQ ID NO: 6144, SEQ ID NO: 6145, SEQ ID NO: 6147, SEQ ID NO: 6154, SEQ ID NO: 6167, SEQ ID NO: 6168, SEQ ID NO: 6170, SEQ ID NO: 6173, SEQ ID NO: 6178, and SEQ ID NO: 6181.

9. A microarray according to claim 8 where at least 75% of the nucleic acid molecules are comprised of different sequences and at least about 250 nucleotide residues and complementary to a molecule comprising a sequence selected from said group.

10. A microarray according to claim 8 where at least 95% of the nucleic acid molecules are comprised of different sequences and at least about 250 nucleotide residues and complementary to a molecule comprising a sequence selected from said group.

Appendix C: Claims as Originally Filed in the Preliminary Amendment of October 10, 2000

8. A microarray having a substrate with a surface comprising 10^3 nucleic acid molecules or more where at least 10% of the nucleic acid molecules are different and at least about 250 nucleotide residues and complementary to a molecule having a sequence selected from the group consisting of SEQ ID NO: 5776 and SEQ ID NO: 5781 and SEQ ID NO: 5782 and SEQ ID NO: 5783 and SEQ ID NO: 5786 and SEQ ID NO: 5787 and SEQ ID NO: 5800 and SEQ ID NO: 5815 and SEQ ID NO: 5818 and SEQ ID NO: 5821 and SEQ ID NO: 5823 and SEQ ID NO: 5828 and SEQ ID NO: 5830 and SEQ ID NO: 5836 and SEQ ID NO: 5838 and SEQ ID NO: 5840 and SEQ ID NO: 5845 and SEQ ID NO: 5849 and SEQ ID NO: 5850 and SEQ ID NO: 5851 and SEQ ID NO: 5859 and SEQ ID NO: 5863 and SEQ ID NO: 5868 and SEQ ID NO: 5874 and SEQ ID NO: 5875 and SEQ ID NO: 5877 and SEQ ID NO: 5893 and SEQ ID NO: 5896 and SEQ ID NO: 5901 and SEQ ID NO: 5909 and SEQ ID NO: 5922 and SEQ ID NO: 5926 and SEQ ID NO: 5928 and SEQ ID NO: 5931 and SEQ ID NO: 5936 and SEQ ID NO: 5937 and SEQ ID NO: 5939 and SEQ ID NO: 5941 and SEQ ID NO: 5950 and SEQ ID NO: 5955 and SEQ ID NO: 5956 and SEQ ID NO: 5963 and SEQ ID NO: 5973 and SEQ ID NO: 5974 and SEQ ID NO: 5991 and SEQ ID NO: 5994 and SEQ ID NO: 5999 and SEQ ID NO: 6000 and SEQ ID NO: 6001 and SEQ ID NO: 6005 and SEQ ID NO: 6006 and SEQ ID NO: 6007 and SEQ ID NO: 6011 and SEQ ID NO: 6017 and SEQ ID NO: 6022 and SEQ ID NO: 6023 and SEQ ID NO: 6030 and SEQ ID NO: 6033 and SEQ ID NO: 6059 and SEQ ID NO: 6065 and SEQ ID NO: 6089 and SEQ ID NO: 6091 and SEQ ID NO: 6106 and SEQ ID NO: 6107 and SEQ ID NO: 6110 and SEQ ID NO: 6117 and SEQ ID NO: 6121 and SEQ ID NO: 6124 and SEQ ID NO: 6137 and SEQ ID NO: 6154 and SEQ ID NO: 6167 and SEQ ID NO: 6168 and SEQ ID NO: 6170 and SEQ ID NO: 6173 and SEQ ID NO: 6178 and SEQ ID NO: 6181 and SEQ ID NO: 6188 and SEQ ID NO: 6195 and SEQ ID NO: 6196 and SEQ ID NO: 6205 and SEQ ID NO: 6211 and SEQ ID NO: 6212 and SEQ ID NO: 6214 and SEQ ID NO: 6234 and SEQ ID NO: 6241 and SEQ ID NO: 6245 and SEQ ID NO: 6251 and SEQ ID NO: 6256 and SEQ ID NO: 6261 and SEQ ID NO: 6270 and SEQ ID NO: 6272 and SEQ ID NO: 6278 and SEQ ID NO: 6283 and SEQ ID NO: 6286 and SEQ ID NO: 6288 and SEQ ID NO: 6289 and SEQ ID NO: 6291 and SEQ ID NO: 6292 and SEQ ID NO: 6293 and SEQ ID NO:

6295 and SEQ ID NO: 6302 and SEQ ID NO: 6309 and SEQ ID NO: 6316 and SEQ ID NO: 6321 and SEQ ID NO: 6324 and SEQ ID NO: 6332 and SEQ ID NO: 6337 and SEQ ID NO: 6347 and SEQ ID NO: 6348 and SEQ ID NO: 6352 and SEQ ID NO: 6355 and SEQ ID NO: 6358 and SEQ ID NO: 6361 and SEQ ID NO: 6363 and SEQ ID NO: 6367 and SEQ ID NO: 6369 and SEQ ID NO: 6371 and SEQ ID NO: 6375 and SEQ ID NO: 6377 and SEQ ID NO: 6385 and SEQ ID NO: 6405 and SEQ ID NO: 6416 and SEQ ID NO: 6418 and SEQ ID NO: 6425 and SEQ ID NO: 6433 and SEQ ID NO: 6445 and SEQ ID NO: 6451 and SEQ ID NO: 6454 and SEQ ID NO: 6459 and SEQ ID NO: 6462 and SEQ ID NO: 6464 and SEQ ID NO: 6465 and SEQ ID NO: 6466 and SEQ ID NO: 6476 and SEQ ID NO: 6479 and SEQ ID NO: 6481 and SEQ ID NO: 6482 and SEQ ID NO: 6483 and SEQ ID NO: 6489 and SEQ ID NO: 6497 and SEQ ID NO: 6502 and SEQ ID NO: 6514 and SEQ ID NO: 6521 and SEQ ID NO: 6529 and SEQ ID NO: 6530 and SEQ ID NO: 6535 and SEQ ID NO: 6540 and SEQ ID NO: 6553 and SEQ ID NO: 6556 and SEQ ID NO: 6564 and SEQ ID NO: 6565 and SEQ ID NO: 6571 and SEQ ID NO: 6598 and SEQ ID NO: 6603 and SEQ ID NO: 6604 and SEQ ID NO: 6606 and SEQ ID NO: 6611 and SEQ ID NO: 6613 and SEQ ID NO: 6620 and SEQ ID NO: 6628 and SEQ ID NO: 6633 and SEQ ID NO: 6639 and SEQ ID NO: 6640 and SEQ ID NO: 6643 and SEQ ID NO: 6651 and SEQ ID NO: 6652 and SEQ ID NO: 6654 and SEQ ID NO: 6657 and SEQ ID NO: 6659 and SEQ ID NO: 6661 and SEQ ID NO: 6664 and SEQ ID NO: 6668 and SEQ ID NO: 6670 and SEQ ID NO: 6671 and SEQ ID NO: 6674 and SEQ ID NO: 6680 and SEQ ID NO: 6685 and SEQ ID NO: 6686 and SEQ ID NO: 6688 and SEQ ID NO: 6691 and SEQ ID NO: 6692 and SEQ ID NO: 6696 and SEQ ID NO: 6697 and SEQ ID NO: 6702 and SEQ ID NO: 6704 and SEQ ID NO: 6711 and SEQ ID NO: 6716 and SEQ ID NO: 6724 and SEQ ID NO: 6726 and SEQ ID NO: 6728 and SEQ ID NO: 6739 and SEQ ID NO: 6742 and SEQ ID NO: 6744 and SEQ ID NO: 6747 and SEQ ID NO: 6764 and SEQ ID NO: 6766 and SEQ ID NO: 6770 and SEQ ID NO: 6772 and SEQ ID NO: 6773 and SEQ ID NO: 6778 and SEQ ID NO: 6781 and SEQ ID NO: 6782 and SEQ ID NO: 6790 and SEQ ID NO: 6792 and SEQ ID NO: 6841 and SEQ ID NO: 6870 and SEQ ID NO: 6871 and SEQ ID NO: 6886 and SEQ ID NO: 6894 and SEQ ID NO: 6904 and SEQ ID NO: 6906 and SEQ ID NO: 6923 and SEQ ID NO: 6931 and SEQ ID NO: 6934 and SEQ ID NO: 6938 and SEQ ID NO: 6939 and SEQ ID NO: 6949 and SEQ ID NO: 6953 and SEQ ID NO: 6961 and SEQ ID NO:

6965 and SEQ ID NO: 6978 and SEQ ID NO: 6991 and SEQ ID NO: 7000 and SEQ ID NO: 7002 and SEQ ID NO: 7036 and SEQ ID NO: 7050 and SEQ ID NO: 7053 and SEQ ID NO: 7062 and SEQ ID NO: 7070 and SEQ ID NO: 7078 and SEQ ID NO: 7083 and SEQ ID NO: 7096 and SEQ ID NO: 7100 and SEQ ID NO: 7106 and SEQ ID NO: 7107 and SEQ ID NO: 7134 and SEQ ID NO: 7144 and SEQ ID NO: 7161 and SEQ ID NO: 7164 and SEQ ID NO: 7178 and SEQ ID NO: 7206 and SEQ ID NO: 7220 and SEQ ID NO: 7221 and SEQ ID NO: 7224 and SEQ ID NO: 7228 and SEQ ID NO: 7229 and SEQ ID NO: 7241 and SEQ ID NO: 7246 and SEQ ID NO: 7248 and SEQ ID NO: 7249 and SEQ ID NO: 7254 and SEQ ID NO: 7261 and SEQ ID NO: 7267 and SEQ ID NO: 7277 and SEQ ID NO: 7332 and SEQ ID NO: 7338 and SEQ ID NO: 7351 and SEQ ID NO: 7357 and SEQ ID NO: 7369 and SEQ ID NO: 7378 and SEQ ID NO: 7380 and SEQ ID NO: 7384 and SEQ ID NO: 7386 and SEQ ID NO: 7395 and SEQ ID NO: 7438 and SEQ ID NO: 7444 and SEQ ID NO: 7447 and SEQ ID NO: 7461 and SEQ ID NO: 7463 and SEQ ID NO: 7465 and SEQ ID NO: 7468 and SEQ ID NO: 7478 and SEQ ID NO: 7490 and SEQ ID NO: 7491 and SEQ ID NO: 7492 and SEQ ID NO: 7509 and SEQ ID NO: 7514 and SEQ ID NO: 7536 and SEQ ID NO: 7559 and SEQ ID NO: 7563 and SEQ ID NO: 7565 and SEQ ID NO: 7572 and SEQ ID NO: 7576 and SEQ ID NO: 7590 and SEQ ID NO: 7592 and SEQ ID NO: 7594 and SEQ ID NO: 7596 and SEQ ID NO: 7602 and SEQ ID NO: 7612 and SEQ ID NO: 7617 and SEQ ID NO: 7618 and SEQ ID NO: 7622 and SEQ ID NO: 7624 and SEQ ID NO: 7627 and SEQ ID NO: 7631 and SEQ ID NO: 7632 and SEQ ID NO: 7644 and SEQ ID NO: 7646 and SEQ ID NO: 7655 and SEQ ID NO: 7657 and SEQ ID NO: 7659 and SEQ ID NO: 7677 and SEQ ID NO: 7682 and SEQ ID NO: 7685 and SEQ ID NO: 7690 and SEQ ID NO: 7694 and SEQ ID NO: 7697 and SEQ ID NO: 7701 and SEQ ID NO: 7702 and SEQ ID NO: 7703 and SEQ ID NO: 7707 and SEQ ID NO: 7708 and SEQ ID NO: 7711 and SEQ ID NO: 7715 and SEQ ID NO: 7718 and SEQ ID NO: 7721 and SEQ ID NO: 7723 and SEQ ID NO: 7724 and SEQ ID NO: 7729 and SEQ ID NO: 7736 and SEQ ID NO: 7745 and SEQ ID NO: 7749 and SEQ ID NO: 7757 and SEQ ID NO: 7761 and SEQ ID NO: 7770 and SEQ ID NO: 7772 and SEQ ID NO: 7777 and SEQ ID NO: 7782 and SEQ ID NO: 7791 and SEQ ID NO: 7795 and SEQ ID NO: 7796 and SEQ ID NO: 7800 and SEQ ID NO: 7801 and SEQ ID NO: 7802 and SEQ ID NO: 7808 and SEQ ID NO: 7809 and SEQ ID NO: 7813 and SEQ ID NO: 7818 and SEQ ID NO: 7823 and SEQ ID NO:

7825 and SEQ ID NO: 7826 and SEQ ID NO: 7827 and SEQ ID NO: 7831 and SEQ ID NO: 7837 and SEQ ID NO: 7844 and SEQ ID NO: 7845 and SEQ ID NO: 7847 and SEQ ID NO: 7849 and SEQ ID NO: 7852 and SEQ ID NO: 7856 and SEQ ID NO: 7860 and SEQ ID NO: 7862 and SEQ ID NO: 7863 and SEQ ID NO: 7865 and SEQ ID NO: 7867 and SEQ ID NO: 7870 and SEQ ID NO: 7872 and SEQ ID NO: 7880 and SEQ ID NO: 7883 and SEQ ID NO: 7884 and SEQ ID NO: 7885 and SEQ ID NO: 7886 and SEQ ID NO: 7888 and SEQ ID NO: 7889 and SEQ ID NO: 7894 and SEQ ID NO: 7895 and SEQ ID NO: 7896 and SEQ ID NO: 7901 and SEQ ID NO: 7905 and SEQ ID NO: 7908 and SEQ ID NO: 7918 and SEQ ID NO: 7928 and SEQ ID NO: 7931 and SEQ ID NO: 7937 and SEQ ID NO: 7947 and SEQ ID NO: 7952 and SEQ ID NO: 7959 and SEQ ID NO: 7962 and SEQ ID NO: 7975 and SEQ ID NO: 7987 and SEQ ID NO: 7989 and SEQ ID NO: 7992 and SEQ ID NO: 7997 and SEQ ID NO: 7998 and SEQ ID NO: 8002 and SEQ ID NO: 8006 and SEQ ID NO: 8007 and SEQ ID NO: 8008 and SEQ ID NO: 8010 and SEQ ID NO: 8015 and SEQ ID NO: 8017 and SEQ ID NO: 8018 and SEQ ID NO: 8020 and SEQ ID NO: 8022 and SEQ ID NO: 8024 and SEQ ID NO: 8026 and SEQ ID NO: 8043 and SEQ ID NO: 8048 and SEQ ID NO: 8053 and SEQ ID NO: 8063 and SEQ ID NO: 8064 and SEQ ID NO: 8066 and SEQ ID NO: 8095 and SEQ ID NO: 8098 and SEQ ID NO: 8099 and SEQ ID NO: 8103 and SEQ ID NO: 8126 and SEQ ID NO: 8145 and SEQ ID NO: 8153 and SEQ ID NO: 8155 and SEQ ID NO: 8157 and SEQ ID NO: 8161 and SEQ ID NO: 8171 and SEQ ID NO: 8175 and SEQ ID NO: 8180 and SEQ ID NO: 8184 and SEQ ID NO: 8192 and SEQ ID NO: 8198 and SEQ ID NO: 8199 and SEQ ID NO: 8201 and SEQ ID NO: 8212 and SEQ ID NO: 8216 and SEQ ID NO: 8222 and SEQ ID NO: 8224 and SEQ ID NO: 8225 and SEQ ID NO: 8228 and SEQ ID NO: 8238 and SEQ ID NO: 8242 and SEQ ID NO: 8256 and SEQ ID NO: 8259 and SEQ ID NO: 8274 and SEQ ID NO: 8277 and SEQ ID NO: 8278 and SEQ ID NO: 8289 and SEQ ID NO: 8292 and SEQ ID NO: 8297 and SEQ ID NO: 8301 and SEQ ID NO: 8317 and SEQ ID NO: 8329 and SEQ ID NO: 8333 and SEQ ID NO: 8334 and SEQ ID NO: 8335 and SEQ ID NO: 8351 and SEQ ID NO: 8355 and SEQ ID NO: 8374 and SEQ ID NO: 8377 and SEQ ID NO: 8379 and SEQ ID NO: 8383 and SEQ ID NO: 8394 and SEQ ID NO: 8406 and SEQ ID NO: 8447 and SEQ ID NO: 8452 and SEQ ID NO: 8455 and SEQ ID NO: 8458 and SEQ ID NO: 8465 and SEQ ID NO: 8468 and SEQ ID NO: 8472 and SEQ ID NO: 8479 and SEQ ID NO: 8482 and SEQ ID NO:

8487 and SEQ ID NO: 8492 and SEQ ID NO: 8500 and SEQ ID NO: 8503 and SEQ ID NO: 8507 and SEQ ID NO: 8511 and SEQ ID NO: 8512 and SEQ ID NO: 8517 and SEQ ID NO: 8518 and SEQ ID NO: 8529 and SEQ ID NO: 8530 and SEQ ID NO: 8538 and SEQ ID NO: 8542 and SEQ ID NO: 8553 and SEQ ID NO: 8554 and SEQ ID NO: 8556 and SEQ ID NO: 8560 and SEQ ID NO: 8568 and SEQ ID NO: 8569 and SEQ ID NO: 8578 and SEQ ID NO: 8579 and SEQ ID NO: 8580 and SEQ ID NO: 8583 and SEQ ID NO: 8584 and SEQ ID NO: 8585 and SEQ ID NO: 8587 and SEQ ID NO: 8590 and SEQ ID NO: 8601 and SEQ ID NO: 8607 and SEQ ID NO: 8611 and SEQ ID NO: 8616 and SEQ ID NO: 8624 and SEQ ID NO: 8625 and SEQ ID NO: 8631 and SEQ ID NO: 8632 and SEQ ID NO: 8639 and SEQ ID NO: 8644 and SEQ ID NO: 8665.

9. A microarray according to claim 8 where at least 75% of the nucleic acid molecules are different and at least about 250 nucleotide residues and complementary to a molecule having a sequence selected from said group.

10. A microarray according to claim 8 where at least 95% of the nucleic acid molecules are different and at least about 250 nucleotide residues and complementary to a molecule having a sequence selected from said group.